

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 1-5, 7-10, 12, 13, 16-22, and 40 are pending and are directed to a method of inducing an immunological response.

Summary of the Office Action

The Office rejects claims 1-5, 7-10, 12, 13, 16, and 40 under 35 U.S.C. § 103(a) as allegedly obvious over Schlam et al. (WO 00/34494) and Pecher (WO 01/24832).

The Office rejects claims 17-22 under 35 U.S.C. § 103(a) as allegedly obvious over Schlam et al. (WO 00/34494), Pecher (WO 01/24832), and Grosenbach et al., *Cancer Research*, 61: 4497-4505 (2001).

These rejections are traversed for the following reasons.

Discussion of the Obviousness Rejections

In response to Applicants' arguments, the Office maintains that the subject matter of the pending claims is obvious in view of the Schlam and Pecher references when considered alone or in further combination with the Grosenbach reference. The obviousness rejections are traversed for the following reasons.

The Schlam reference indicates that poxvirus vector can encode more than one tumor associated antigen; however, the Schlam reference does not disclose a poxvirus vector encoding MUC and CEA or a prime-boost protocol employing two poxvirus vectors encoding MUC and CEA, as required by the pending claims. Although the Pecher reference discloses a composition comprising a vector (e.g., plasmid) encoding MUC1 and a vector (e.g., plasmid) encoding CEA, the Pecher reference does not disclose any working examples wherein the vectors are administered together. Instead, the Pecher reference describes an experiment wherein an adenovirus vector encoding MUC1 is administered to a mouse followed by administration 14 days later of a plasmid encoding MUC1. In other words, in the experiment of the Pecher reference, a vector encoding only one tumor associated antigen (MUC) was used. Similarly, the Grosenbach reference discloses administration of only one

tumor associated antigen (CEA), which is in combination with costimulatory molecules (TRICOM).

As discussed in the previous replies to Office Actions, the prior art discloses that the presentation of two antigens together (at the same location) was thought to result in competition between the two antigens with one antigen being dominant, thereby resulting in a reduced immune response to one or both of the antigens (see paragraph 7 of the “Declaration Under 37 C.F.R. § 1.132 of Jeffrey Schlom, Ph.D.” submitted herewith). Thus, the impact of administering two antigens together at one location could not have been known without extensive experimentation, such as by designing and implementing a clinical study or, at the very least, a mouse model system for breast cancer (see paragraph 7 of the Rule 132 Declaration). None of the cited references discloses the results of presenting the CEA and MUC antigens together (see paragraph 5 of the Rule 132 Declaration).

The inventors surprisingly discovered that the inventive methods that employ a poxvirus vector encoding CEA and MUC result in the beneficial effect of stimulating the immune system to target both the CEA and MUC antigens without antigenic competition. In particular, the specification describes a Phase I clinical trial, which established the preliminary safety and efficacy profiles of targeted cancer immunotherapy using a prime-boost protocol in cancer patients (see paragraph 8 of the Rule 132 Declaration). The post-filing Mohebtash et al. (*Clin. Cancer Res.*, 17(22): 7164-7173 (2011); submitted herewith), Gulley (*Clin. Cancer Res.*, 14(10): 3060-3069 (2008); of record), and Tsang (*Clin. Cancer Res.*, 11: 1597-1607 (2005); of record) references confirm the efficacy of the inventive methods.

In particular, the Mohebtash, Gulley, and Tsang references demonstrate that the inventive methods result in the development of an increase in antigen-specific (MUC and CEA) immune response and provide a clinical benefit without incidence of antigenic competition (see paragraphs 8-10 of the Rule 132 Declaration).

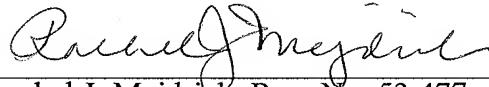
The benefits attendant the present invention are unexpected and surprising in view of the teachings in the prior art at the earliest priority date of the application (e.g., the Palmowski and Brody references). Accordingly, the subject matter of the pending claims would not have been obvious to one of ordinary skill in the art at the relevant time in view of

the combined disclosures of two or more of the Schlom, Pecher references, and Grosenbach references. For the above-described reasons, the obviousness rejections should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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